group, a conjugate group, hydrogen, halogen, hydroxyl, thiol, keto, carboxyl, NR^1R^2, $CONR^1$, amidine, guanidine, glutamyl, nitro, nitrate, nitrile, trifluoromethyl, trifluoromethoxy, NH-alkyl, N-dialkyl, O-aralkyl, S-aralkyl, NH-aralkyl, azido, hydrazino, hydroxylamino, sulfoxide, sulfone, sulfide, disulfide, silyl, a nucleosidic base, an amino acid side chain, a carbohydrate, a drug or a group capable of hydrogen bonding.

In claims 2-8, 12-17, 19 and 24-26, please delete "claim 31" and insert --claim 32-- therefor.

REMARKS

Claim 31 has been canceled.

Claims 2-8, 12-17, 19 and 24-26 have been amended.

Claim 32 has been added. Support for the subject matter recited in this claim is found in Examples 90-94, on pages 110-113. No new matter has been added.

Claims 2-19, 24-26 and 32 are pending in this application.

Claims 2-19, 24-26 and 31 have been rejected under 35 U.S.C. § 101 for allegedly having no utility. As claim 31 includes structure V which shows a pentavalent carbon structure, claim 31 has been canceled. Claim 32 has been added instead, which indicates the correct formula of structure V. Accordingly, this rejection is now moot.

Claims 2-19, 24-26 and 31 have been rejected under 35 U.S.C. § 112, ¶ 1, for allegedly containing subject matter not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor was in possession of the claimed invention. The Office Action states that the chemical structures recited in claim 31 do not appear to be described in the specification.

Although claim 31 has been canceled, Applicant respectfully points out that the chemical structures recited in claim 31 (and now in claim 32) are amply described in the specification. For example, pyrimidine compounds such as structures I, II and III are described in Examples 95-117, page 113, line 8, to page 123, line 8. Furthermore, purine compounds according to the present invention, having structures IV and V, are described in Examples 4-94, on page 58, line 13, to page 113, line 7. Because the claims include structural representations of compounds of the claimed invention, for convenience and ease of prosecution, Applicant has amended the specification to include these structural representations.

The Office Action further states that the formula for the tether "T" does not appear to be supported in the specification. Applicant respectfully points out that the tether is taught in the specification, on page 3, line 27, to page 4, line 3, and also on page 5, line 25, to page 6, line 2. The specification states that

the tether may be, among other forms, straight chain, branched, cyclic or heterocyclic. These terms are defined in the specification, on page 16, lines 17-34. Accordingly, "T" is well defined in the specification.

Claims 7, 9, 11, 12 and 17-19 stand rejected under 35 U.S.C. § 112, ¶ 2, for allegedly being indefinite. Claims 7 and 9 have been rejected for the alleged indefiniteness of the term "nucleophilic." Claims 7 and 9 are directed to mixtures where the functionalizable atom is nucleophilic. The term "nucleophilic" thus defines the nature of the functionalizable atom, and means that this atom is an electron donor. It is well known to the art-skilled that "nucleophilic" indicates a species that gives up or shares electrons with another molecule or ion. Thus the art-skilled would recognize that a nucleophilic species possesses one or more electron-rich sites such as an unshared pair of electrons or *pi*-electrons. Indeed, just such a definition is provided by the McGraw-Hill Dictionary of Scientific and Technical Terms (Fifth ed.), a copy of the relevant portion of this reference being hereby provided. Accordingly, claims 7 and 9 are not indefinite.

Claims 11 and 12 stand rejected for the alleged indefiniteness of the term "electrophilic." Once again, the term "electrophilic" defines the nature of the functionalizable atom, and means that this atom is electron-deficient. It is well known to the art-skilled that "electrophilic" indicates a species that accepts a

pair of electrons from another molecule. Thus the art-skilled would recognize that an electrophilic species is electron-deficient and accepts electrons from electron-rich species. Indeed, the McGraw-Hill Dictionary of Scientific and Technical Terms (Fifth ed.), describes "electrophilic" as referring to an electron-deficient species. A copy of the relevant portion of this reference is hereby provided. Accordingly, claims 11 and 12 are not indefinite.

As the art-skilled will recognize, the terms "nucleophilic" and "electrophilic," as recited in the claims, refer to the electron-rich or electron-deficient nature of the functionalizable atom, not the external conditions under which the functionalizable atom may react with other molecules or species. Accordingly, Applicant respectfully requests that this rejection of claims 7, 9, 11 and 12 be withdrawn.

Claims 17 and 18 stand rejected for allegedly being indefinite. The Office Action states that these claims are vague and indefinite because it is unclear what chemical substituents are being referred to. Applicant respectfully points out that the specification, on page 12, line 1 to page 14, line 30 describes the chemical substituents encompassed by the present invention. The art-skilled would recognize that the chemical substituents taught in the specification can indeed be used in the present invention. Therefore, the conclusion that it is not possible to determine the

metes and bounds of the invention is erroneous. Accordingly, Applicant respectfully requests that this rejection of claims 17 and 18 be withdrawn.

Claim 19 stands rejected for allegedly being indefinite. It is indicated in the Office Action that the claim does not explicitly state the substituents to be utilized so as to obtain ring-opened, ring-closed or bicyclized compounds. Applicant respectfully points out that substituents which may be chosen in order to provide ring-opened, ring-closed or bicyclized compounds are within common knowledge of the art-skilled. The specification, on page 12, line 1, to page 14, line 30, provides the art-skilled with a choice of chemical substituents that may be used. Therefore, the metes and bounds of the present invention are clearly determinable. Accordingly, as claim 19 is not indefinite, Applicant respectfully requests that this rejection be withdrawn.

Claims 2, 3, 5, 13-15 and 31 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Michnick *et al.* (hereinafter "Michnick"). The Office Action states that Michnick teaches pharmaceutical compositions that are comprised of one or a plurality of inventive compounds. The compounds disclosed by Michnick are different from those claimed in the subject application. Michnick discloses N_1-, N_3- and N_7-substituted purines and N_1- and N_3-substituted pyrimidines. Quite different from Michnick's compounds, the claimed mixtures are directed to C_2-, C_4-,

C_8- and N_9-substituted purines and C_2-, C_4- and C_6-substituted pyrimidines. As such, Michnick does not disclose the claimed mixtures. Accordingly, this rejection of the claims is inappropriate, and Applicant respectfully requests that it be withdrawn.

Claims 2-15, 24-26 and 31 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Summerton *et al.* (hereinafter "Summerton"). Summerton teaches morpholino-subunit polymer compositions. The compounds described in the Summerton reference have a morpholino backbone with 1'-substitutions on the morpholine ring. These substitutions are varied to form different compounds. According to Summerton, this 1'-substituent could be a purine or pyrimidine. However, attachment of such substituents to the morpholino moiety is through the N_9 of the purine or the N_1 of the pyrimidine (Summerton, column 7, lines 39-41).

In contrast, Applicant's invention teaches scaffolds that are purines and pyrimidines. The purine or pyrimidine scaffolds are then substituted with various chemical substituents to form a mixture of chemical compounds. However, even if Summerton is construed to describe a purine or pyrimidine substituent at the 1'-position of the morpholine backbone, Summerton does not teach compounds of the present invention. Compounds of the present invention are directed to purines that are substituted at the C_2- and C_4-positions and at the C_2-, C_4-, C_8- and N_9-positions. The

present invention also provides pyrimidines that are substituted at the C_2-, C_4- and C_6-positions. Accordingly, Summerton does not disclose compounds of the mixtures of the present invention. Therefore, Applicant submits that this rejection is inappropriate and should be withdrawn.

Claims 2,3, 5-15, 17-19, 24-26 and 31 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Pavia *et al.* (hereinafter "Pavia"). The Office Action states that Pavia reads on the compounds of the present invention because one ring in Pavia's compound can be a pyrimidine ring and the second ring can be a heterocycle. Applicant respectfully points out that Pavia discloses compounds comprising two rings wherein both rings are aromatic or unsaturated. Further, Pavia's compounds exclude purines.

In contrast, the present invention is directed to mixtures wherein the pyrimidine compounds may be substituted with, among other substituents, saturated heterocycles. Unsaturated or aromatic heterocyclic substituents are not included in the present invention. Accordingly, the mixtures of the present invention comprise compounds that are not disclosed by Pavia. Therefore, as this rejection of the claims is inappropriate, Applicant respectfully requests that it be withdrawn.

In view of the foregoing, Applicant submits that the claims presently before the Examiner patentably define the invention over the applied art and are otherwise in condition for ready allowance. An early Office Action to that effect is, therefore, earnestly solicited.

Respectfully submitted,

John W. Caldwell
Registration No. 28,937

Rena Patel, Ph.D.
Registration No. 41,412

Date: **April 7, 1999**

WOODCOCK WASHBURN KURTZ
MACKIEWICZ & NORRIS
One Liberty Place - 46th Floor
Philadelphia, PA 19103
(215) 568-3100